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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,808	HAN ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-40 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 August 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 2, 8, 16, 25, 33, 35, and 38-40 are rejected under 35 U.S.C. 102(a) as being anticipated by Sanders et al. WO 02/48177 A10 ("Sanders").

Sanders discloses a multidimensional electrophoresis device (16), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See

the abstract and page 05, lines 04-24. Note that claims 1 and 2 do not actually require polyacrylamide gel only that the device be capable of holding such a gel, which the device of Sanders is since the microchannel contains a separation gel throughout its length. Note also the disclosure of SDS on page 6, first full paragraph. For claim 16 note that a loading structure is implied by page 05, lines 25-26, which discloses introducing sample into the end of the focusing section 14. For claim 33 also see page 01: 01-06. For claim 35 also see the abstract and page 05, line 25 – page 06, line 06. For claims 38 and 40 also see page 06, lines 08-15. For claim 39 also see page 05, lines 26-27, which discloses introducing sample in the end of the focusing section.

3. Claims 1, 2, 8, 16-18, 25, and 33 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wiktorowicz et al. (US 6,214,191 B1) ("Wiktorowicz").

Addressing claims 1 and 25, Wiktorowicz discloses a multidimensional electrophoresis device (100), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 4; col. 06: 27-38; col. 07:25-30; col. 07:63-67; col. 09:58 – col. 10:08; and col. 13:66 – col. 14:34.

Addressing claims 2 and 8, for the additional limitation of this claim see col. 16:24-39; and col. 13:66 – col. 14:24.

Addressing claims 16 and 17, for the additional limitations of these claims see col. 07:25-30 and Figure 4.33

Addressing claim 18, for the additional limitation of this claim note channel 160 in Figure 4.

Addressing claim 33, for the additional limitation of this claim see the abstract.

4. Claims 1, 2, 8, 12, 16-22, 25, and 38-40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Manz et al. (US 5,599,432) ("Manz").

Addressing claims 1 and 25, Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Addressing claims 2 and 8, for the additional limitation of this claim see col. 03:18-24; col. 09:33-55; and col. 02:06-36.

Addressing claim 12, for the additional limitation of this claim see claim 11 of Manz.

Addressing claims 16 and 17, for the additional limitations of these claims see col.07:09-12 and Figure 1. Note that inlet 1 is in fluid communication with several microchanels and is thus shared with at two microchannels.

Addressing claim 18, for the additional limitation of this claim note left channel "1" in Figure 1.

Addressing claims 19 and 20, for the additional limitations of these claims note channel "21" in Figure 1. Note that claim 20 does not actually require one of the listed materials.

Addressing claim 21, for the additional limitation of this claim note right channel "1" in Figure 1.

Addressing claim 22, for the additional limitation of this claim note injection device "3" in Figure 1 and see col. 06:61-66 and col. 07:13-30. Note that claim 22 does not require the step of processing the sample.

Addressing claims 38 and 40, for the additional limitations of these claims see col. 02:06-36, note SDS.

Addressing claim 39, for the additional limitation of this claim see col. 07:30-37.

5. Claims 1-5, 8, 12, 16-27, and 33 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Lee et al. (US 6,974,526 B2) ("Lee").

Addressing claims 1 and 25, Lee discloses a multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19.

Addressing claims 2 and 8, for the additional limitation of this claim see col. 03:08-13.

Addressing claims 3-5, for the additional limitations of these claims see col. 05:17-30.

Addressing claim 12, for the additional limitation of this claim see col. 08:05-19.

Addressing claims 16 and 17, for the additional limitations of these claims see col. 04:48-51 and Figures 1-10.

Addressing claim 18, for the additional limitation of this claim note channel "3" in Figures 2-9.

Addressing claims 19 and 20, for the additional limitations of these claims see col. 06:07-11.

[illegible]

Addressing claim 21, for the additional limitation of this claim note the embodiments in Figures 8 and 10 in which channels "4" and "11" are grouped in threes or fours. One of each group of three or four channels can be construed as a bypass channel for the other channels in the group.

Addressing claim 23, for the additional limitation of this claim see col. 06:07-12.

[illegible]

Addressing claims 24 and 26, for the additional limitations of this claims see col. 02:20-33 and col. 07:52-65.

Addressing claim 27, for the additional limitation of this claim note that the membrane is a polymeric strip that lies across the underlying channels. See Figure 10. If pressure were applied to the membrane it would any channels under the region in which pressure was applied.

Addressing claim 33, for the additional limitations of this claims see the abstract.

Addressing claims 38-40, for the additional limitations of these claims see col. 05:45-49 and col. 06:13-20.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 3-7 and 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanders et al. WO 02/48177 A10 ("Sanders").

Addressing claims 3-7, Sanders discloses a multidimensional electrophoresis device (16), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract and page 05, lines 04-24. Note that claims 1

and 2 do not actually require polyacrylamide gel only that the device be capable of holding such a gel, which the device of Sanders is since the microchannel contains a separation gel throughout its length. Note also the disclosure of SDS on page 6., first full paragraph.

Sanders does not mention having the length be within the claimed ranges; however, Sanders does disclose having the device be only 20 mm x 40 mm and that the microchannel may be straight or curved. See page 10, lines 16-19 and page 03, lines 23-24. Thus, barring evidence to the contrary, such as unexpected results, the claimed length ranges are either arbitrary, or just a matter of optimizing the microchannel length for improved separation to provide a smaller pH gradient, that is many isoelectric sections, or to increase the separation path for the gel electrophoresis, which will improve the resolution of the sample components.

Addressing claims 28-32, Sanders does not mention the time for performing IEF, SDS-PAGE, or native PAGE, although Sanders does disclose measuring analyte velocity. See page 09, second full paragraph. However, barring evidence to the contrary, such as unexpected results, the time for performing one of these separations will depend on the desired resolution and separation conditions optimized for this resolution. For example, it was known in the art that the higher the electrophoresis voltage the quicker the separation, however, resolution would be adversely affected at higher voltages because of Joule heating. Also, a shorter microchannel lengths will

reduce the separation time however the separation resolution will not be as great as for longer microchannels, other things being equal.

10. Claims 3-7, 28-33, 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiktorowicz et al. (US 6,214,191 B1) ('Wiktorowicz").

Addressing claims 3-7, Wiktorowicz discloses a multidimensional electrophoresis device (100), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 4; col. 06: 27-38; col. 07:25-30; col. 07:63-67; col. 09:58 – col. 10:08; and col. 13:66 – col. 14:34.

Wiktorowicz does not mention the claimed length ranges; however, Wiktorowicz does disclose that the separation cavity length may be 1 to 20 centimeters, which overlaps or has a shared end point with at least the ranges of claims 3-5. See col. 08:06-29. Since Wiktorowicz also discloses that the channel widths may be only 0.25mm, barring evidence to the contrary, such as unexpected results, the claimed length ranges are either arbitrary, or just a matter of optimizing the microchannel length for improved separation to provide a smaller pH gradient, that is many isoelectric sections, or to increase the separation path for the gel electrophoresis, which will improve the resolution of the sample components.

Addressing claims 28-32, Wiktorowicz does not mention the time for performing IEF, SDS-PAGE, or native PAGE. However, barring evidence to the contrary, such as unexpected results, the time for performing one of these separations will depend on the desired resolution and separation conditions optimized for this resolution. For example, it was known in the art that the higher the electrophoresis voltage the quicker the separation, however, resolution would be adversely affected at higher voltages because of Joule heating. Also, a shorter microchannel lengths will reduce the separation time however the separation resolution will not be as great as for longer microchannels, other things being equal.

Addressing claim 33, Wiktorowicz does not mention a sample comprising protein; however, it would have been obvious to one with ordinary skill in the art at the time of the invention to use the device with a sample comprising at least one protein because Wiktorowicz discloses isoelectric focusing is commonly used for protein separations.

Addressing claims 35, Wiktorowicz discloses a multidimensional electrophoresis device (100), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 4; col. 06: 27-38; col. 07:25-30; col. 07:63-67; col. 09:58 – col. 10:08; and col. 13:66 – col. 14:34.

Wiktorowicz clearly intends for the device to be used. See the abstract and col. 04:03-25 and col. 12:10-16.

11. Claims 3-7, 28-32, 34, 35, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al. (US 5,599,432) ("Manz").

Addressing claims 3-7, Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Manz does not mention the claimed length ranges; however, Manz discloses that the channel widths may be only 1 micron wide. See col. 05:55-58. So barring evidence to the contrary, such as unexpected results, the claimed length ranges are either arbitrary, or just a matter of optimizing the microchannel length for improved separation to provide a smaller pH gradient, that is many isoelectric sections, or to increase the separation path for the gel electrophoresis, which will improve the resolution of the sample components.

Addressing claims 28-32, Manz does not mention the time for performing IEF, SDS-PAGE, or native PAGE, although Manz notes that capillary electrophoresis can be performed under one minute in microchips. See col. 02:61-66. However, barring evidence to the contrary, such as unexpected results, the time for performing one of these separations will depend on the desired resolution and separation conditions optimized for this resolution. For example, it was known in the art that the higher the electrophoresis voltage the quicker the separation, however, resolution would be adversely affected at higher voltages because of Joule heating. Also, a shorter microchannel lengths will reduce the separation time however the separation resolution will not be as great as for longer microchannels, other things being equal.

Addressing claim 34, Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Manz also discloses conducting IEF in at least one horizontal channel 3 – Figure 6) between two electrodes (in reservoirs 5 and 6) and SDS-PAGE or PAGE in at least one vertical channel (11) between two pairs of electrodes (in reservoirs 35 and 37), wherein one pair of the electrodes is placed above the two electrodes of the horizontal microchannel and the other pair of electrodes is placed below the two electrodes

(Figure 6). See also col. 05:61 – col. 06:04 and col. 10:44-49. Manz does not mention conducting IEF when the electrodes on the right side are of one voltage and the electrodes on the left side are of another voltage preventing the fluid sample from migrating through the vertical microchannel. However, it would have been obvious to one with ordinary skill in the art at the time of the invention to do so because this will allow the sample to undergo complete IEF separation before undergoing PAGE. If the two pairs of electrodes were at voltages that allowed migration through a vertical channel then sample components focused along the IEF channel at the intersections with the vertical channel would be separated in the vertical channel before the sample was completely separated by IEF. This may adversely affect the electrical field along the IEF channel because of competing fields and changing ionic strength in the vertical channel.

Addressing claims 35 and 37, Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Manz clearly intends for the device to be used. See the abstract and col. 03:25-57.

12. Claims 6, 7, 28-32, 35, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee").

Addressing claims 6 and 7, Lee discloses a multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19.

Lee does not mention the claimed length ranges; however, Lee discloses that the channel widths may be only 5 microns wide and "The microchannels (e.g. **3**, **4**) can be nay suitable length." See col. 05:17-30. So barring evidence to the contrary, such as unexpected results, the claimed length ranges are either arbitrary, or just a matter of optimizing the microchannel length for improved separation to provide a smaller pH gradient, that is many isoelectric sections, or to increase the separation path for the gel electrophoresis, which will improve the resolution of the sample components.

Addressing claims 28-32, Lee does not mention the time for performing IEF, SDS-PAGE, or native PAGE. See col. 02:61-66. However, barring evidence to the contrary, such as unexpected results, the time for performing one of these separations will depend on the desired resolution and separation conditions optimized for this resolution. For example, it was known in the art that the higher the electrophoresis voltage the quicker the separation, however, resolution would be adversely affected at higher voltages because of Joule heating. Also, a shorter microchannel lengths will

reduce the separation time however the separation resolution will not be as great as for longer microchannels, other things being equal.

Addressing claims 35 and 36, Lee discloses a multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19. Lee also discloses having the polymeric membrane be placed on top of the microchannel. See col. 02:20-33 and col. 07:52-65.

Lee clearly intends for the device to be used. See the abstract and col. 02:01 – 03:20.

13. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee") in view of Mathies et al. (US 6,623,613 B1) ("Mathies").

Addressing claim 12, Lee discloses a multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19.

Lee does not mention having the plurality of microchanels comprise different solid sieving materials. However, Lee does discloses that for a particularly microfluidic network the solid sieving materiel may be selected form a variety for sieving materials. See col. 06:60-62.

Mathies discloses providing a plurality of independent microfluidic networks on a substrate. See the abstract and Figure 4.

It would have been obvious to one with ordinary skill in the art at the time of the invention to provide a plurality of microfluidic networks and thus microchannels as taught by Mathies in the invention of Lee because then a plurality of samples can be simultaneously analyzed.

It would have been further obvious to one with ordinary skill in the art at the time of the invention to use different solid sieving materials in at least some of the plurality of microfluidic networks because this will help optimize the microfluidic networks for analyzing different samples.

14. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee") in view of Mathies et al. (US 6,623,613 B1) ("Mathies") as applied to claim 12 above, and further in view of Heller (US 6,488,832 B2).

Lee as modified by Mathies does not disclose having the solid sieving materials

be of varying concentrations of at least one polymer between about 4% to about 20%(wt/vol).

Heller discloses, "Gradient gel electrophoresis is a technique in which a gel matrix having an increasing concentration of polyacrylamide (3% to 40%) along the separation axis is used to separate macromolecules in a wide range of sizes." See col. 02:53 – col. 03:55.

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the solid sieving materials be of varying concentration as taught by Heller in the invention of Lee as modified by Mathies because this will optimize the separation conditions for the samples. For example, Heller discloses that DNA separation can be optimized with a solid sieving material of varying concentration. See col. 03:06-56. As for the concentration being between about 4% to about 20%, this is within the range disclosed by Heller and so barring a showing of unexpected results just further optimization of the sieving material for the expected sample types.

15. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanders et al. WO 02/48177 A10 ("Sanders") in view of Woudenberg et al. (US 6,660,147 B1) (Woudenberg") and Zhang et al. (US 6,464,850 B1) ("Zhang").

Sanders discloses a multidimensional electrophoresis device (16), for isoelectric

focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract and page 05, lines 04-24. Note that claims 1 and 2 do not actually require polyacrylamide gel only that the device be capable of holding such a gel, which the device of Sanders is since the microchannel contains a separation gel throughout its length. Note also the disclosure of SDS on page 6., first full paragraph.

Sanders does not mention how the sieving material is made, particularly whether UV-initiated polymerization is used or the photoinitiator of claim 11. As a first matter, the additional limitations of claims 9 and 11 are product-by-process limitations that do not structurally or compositionally differentiate the solid sieving material from that of Sanders without some showing by Applicants. In any event, as shown by Woudenberg a variety of sieving materials such as UV-initiated polymerized polyacrylamide were used as electrophoresis media in a microchannel (see the abstract and col. 08:35-60) and as shown by Zhang a variety of initiators, such as 2,2'-Azobis(2-amidinopropane) dihydrochloride were known at the time of the invention for making electrophoresis media (abstract and col. 11:33-65). So, barring evidence to the contrary, such as unexpected results, the choice of gel, such as polyacrylamide from known electrophoresis media (sieving material) will just depend on the analyte and the separation conditions and the choice of how electrophoresis medium is made will depend on the electrophoresis medium chosen.

16. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiktorowicz et al. (US 6,214,191 B1) ('Wiktorowicz") in view of Woudenberg et al. (US 6,660,147 B1) (Woudenberg") and Zhang et al. (US 6,464,850 B1) ("Zhang").

Wiktorowicz discloses a multidimensional electrophoresis device (100), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 4; col. 06: 27-38; col. 07:25-30; col. 07:63-67; col. 09:58 – col. 10:08; and col. 13:66 – col. 14:34.

Wiktorowicz does not mention how the sieving material is made, particularly whether UV-initiated polymerization is used or the photoinitiator of claim 11, although Wiktorowicz does disclose a variety of possible sieving materials including polyacrylamide. See col. 13: 66 – col. 14:24. As a first matter, the additional limitations of claims 9 and 11 are product-by-process limitations that do not structurally or compositionally differentiate the solid sieving material from that of Wiktorowicz without some showing by Applicants. In any event, as shown by Woudenberg a variety of sieving materials such as UV-initiated polymerized polyacrylamide were used as electrophoresis media in a microchannel (see the abstract and col. 08:35-60) and as shown by Zhang a variety of initiators, such as 2,2'-Azobis(2-amidinopropane) dihydrochloride were known at the time of the invention for making electrophoresis media (abstract and col. 11:33-65). So, barring evidence to the contrary, such as unexpected results, the choice of gel, such as polyacrylamide from known electrophoresis media (sieving material) will just depend on the analyte and the

separation conditions (Wiktorowicz col. 13:66 – col. 14:24) and the choice of how electrophoresis medium is made will depend on the electrophoresis medium chosen.

17. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al. (US 5,599,432) ("Manz") in view of Woudenberg et al. (US 6,660,147 B1) (Woudenberg") and Zhang et al. (US 6,464,850 B1) ("Zhang").

Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Manz does not mention how the sieving material is made, particularly whether UV-initiated polymerization is used or the photoinitiator of claim 11, although Manz does disclose that a variety of sieving materials may be used including polyacrylamide. See col. 09:33–42; col. 06:12-25; and col. 02:06-18. As a first matter, the additional limitations of claims 9 and 11 are product-by-process limitations that do not structurally or compositionally differentiate the solid sieving material from that of Manz without some showing by Applicants. In any event, as shown by Woudenberg a variety of sieving materials such as UV-initiated polymerized polyacrylamide were used as electrophoresis media in a microchannel (see the abstract and col. 08:35-60) and as

shown by Zhang a variety of initiators, such as 2,2'-Azobis(2-amidinopropane) dihydrochloride were known at the time of the invention for making electrophoresis media (abstract and col. 11:33-65). So, barring evidence to the contrary, such as unexpected results, the choice of gel, such as polyacrylamide from known electrophoresis media (sieving material) will just depend on the analyte and the separation conditions (Manz col. 09:40-46) and the choice of how electrophoresis medium is made will depend on the electrophoresis medium chosen.

18. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee") in view of Woudenberg et al. (US 6,660,147 B1) (Woudenberg") and Zhang et al. (US 6,464,850 B1) ("Zhang").

Lee discloses a multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19.

Lee does not mention how the sieving material is made, particularly whether UV-initiated polymerization is used or the photoinitiator of claim 11, although Lee does a variety of possible sieving materials including polyacrylamide. See col. 03:08-13 and claim 12. As a first matter, the additional limitations of claims 9 and 11 are product-by-

process limitations that do not structurally or compositionally differentiate the solid sieving material from that of Lee without some showing by Applicants. In any event, as shown by Woudenberg a variety of sieving materials such as UV-initiated polymerized polyacrylamide were used as electrophoresis media in a microchannel (see the abstract and col. 08:35-60) and as shown by Zhang a variety of initiators, such as 2,2'-Azobis(2-amidinopropane) dihydrochloride were known at the time of the invention for making electrophoresis media (abstract and col. 11:33-65). So, barring evidence to the contrary, such as unexpected results, the choice of gel, such as polyacrylamide from known electrophoresis media (sieving material) will just depend on the analyte and the separation conditions and the choice of how electrophoresis medium is made will depend on the electrophoresis medium chosen.

19. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manz et al. (US 5,599,432) ("Manz") in view of Heller (US 6,488,832 B2).

Manz discloses a multidimensional electrophoresis device (Figure 1), for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figure 1; col. 05:55-59; col. 05:13-27; col. 07:66 – col. 08:12; col. 09:33-54; col. 03:18-23; and col. 02:06-36.

Manz also discloses providing different solid sieving materials. See claim 11 of Manz.

Manz does not disclose having the solid sieving materials be of varying concentrations of at least one polymer between about 4% to about 20%(wt/vol).

Heller discloses, "Gradient gel electrophoresis is a technique in which a gel matrix having an increasing concentration of polyacrylamide (3% to 40%) along the separation axis is used to separate macromolecules in a wide range of sizes." See col. 02:53 – col. 03:55.

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the solid sieving materials be of varying concentration as taught by Heller in the invention of Manz because this will optimize the separation conditions for the samples. For example, Heller discloses that DNA separation can be optimized with a solid sieving material of varying concentration. See col. 03:06-56. As for the concentration being between about 4% to about 20%, this is within the range disclosed by Heller and so barring a showing of unexpected results just further optimization of the sieving material for the expected sample types.

20. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee") in view of Mathies et al. (US 6,623,613 B1) ("Mathies") in view of Heller (US 6,488,832 B2).

Lee as modified by Mathies does not disclose having the solid sieving materials be of varying concentrations of at least one polymer between about 4% to about 20%(wt/vol).

Heller discloses, "Gradient gel electrophoresis is a technique in which a gel matrix having an increasing concentration of polyacrylamide (3% to 40%) along the separation axis is used to separate macromolecules in a wide range of sizes." See col. 02:53 – col. 03:55.

It would have been obvious to one with ordinary skill in the art at the time of the invention to have the solid sieving materials be of varying concentration as taught by Heller in the invention of Lee as modified by Mathies because this will optimize the separation conditions for the samples. For example, Heller discloses that DNA separation can be optimized with a solid sieving material of varying concentration. See col. 03:06-56. As for the concentration being between about 4% to about 20%, this is within the range disclosed by Heller and so barring a showing of unexpected results just further optimization of the sieving material for the expected sample types.

21. Claim 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US 6,974,526 B2) ("Lee") in view of Andersson et al. (US 6,812,456 B2) ("Andersson").

Lee discloses a kit comprising multidimensional electrophoresis device, for isoelectric focusing (IEF), or polyacrylamide gel electrophoresis (PAGE), or both of a fluid sample, comprising at least one microchannel having a length and a solid sieving material. See the abstract; Figures 2-9; col. 05:26-30; col. 01:25-37; col. 05:46-49; and col. 12:13-19.

Lee also discloses including in the kit at least one reagent necessary for conducting IEF of PAGE separations. See col. 05:45-49 and col. 06:13-20.

Lee does not mention injecting the fluid sample into the multidimensional device.

Andersson discloses a kit comprising multidimensional microfluidic device for analyzing fluid and means for injecting the fluid sample into the multidimensional device. See the abstract and col. 20:36-46. It would have been obvious to one with ordinary skill in the art to include in the kit of Lee the means for injecting fluid sample as taught by Andersson because then the sample and reagents can be automatically and accurately injected in the device.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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